

WHAT IS CLAIMED IS:

1. Method for the production of recombinant DNA-derived tissue plasminogen activator (tPA), a tPA variant, a Kringle 2 Serine protease molecule (K2S) or a K2S variant in prokaryotic cells, wherein said tPA, tPA variant, K2S molecule or K2S variant is secreted extracellularly as an active and correctly folded protein, characterized in that the prokaryotic cell contains and expresses a vector comprising the DNA coding for said tPA, tPA variant, K2S molecule or K2S variant operably linked to the DNA coding for the signal peptide OmpA or a functional derivative thereof.

2. Method according to claim 1, characterised in that said the prokaryotic cell contains and expresses a vector comprising the DNA coding for said tPA, tPA variant, K2S molecule or K2S variant operably linked to the DNA coding for the signal peptide OmpA which is operably linked to the nucleic acid molecule defined by the sequence TCTGAGGGAAACAGTGAC (SEQ ID NO:1) or a functional derivative thereof.

3. Method according to claim 1 or 2, characterised in that the prokaryotic cell is *E. coli*.

4. Method according to one of claims 1 to 3, characterised in that the the following steps are carried out:

- a) the DNA encoding the tPA, tPA variant, K2S molecule or K2S variant is amplified by PCR;
- b) the PCR product is purified;
- c) said PCR product is inserted into a vector comprising the DNA coding for OmpA signal peptide and the DNA coding for gpIII in such a way that said PCR product is operably linked upstream to the DNA coding for the OmpA signal sequence and linked downstream to the DNA coding for gpIII of said vector;

- d) that a stop codon is inserted between said tPA, tPA variant, K2S molecule or K2S variant and gpIII;
- e) said vector is expressed by the prokaryotic cell;
- f) the tPA, tPA variant, K2S molecule or K2S variant is purified.

5. Method according to one of claims 1 to 4, characterised in that the vector is a phagemid vector comprising the DNA coding for OmpA signal peptide and the DNA coding for gpIII.

6. Method according to one of claims 1 to 5, characterised in that the vector is the pComb3HSS phagemid.

7. Method according to one of claims 1 to 6, characterised in that the DNA Sequence of OmpA linked upstream to K2S comprises the following sequence or a functional variant thereof or a variant due to the degenerate nucleotide code:

ATGAAAAAGACAGCTATCGCGATTGCAGTGGCACTGGCTGGTTTCG
CTACCGTGGCCCAGGCGGCCTCTGAGGGAAACAGTGACTGCTACTT
TGGGAATGGGTCAGCCTACCGTGGCACGCACAGCCTCACCGAGTCG
GGTGCCTCCTGCCTCCCGTGGAATTCCATGATCCTGATAGGCAAGG
TTTACACAGCACAGAACCCCAAGTGCCCAGGCACTGGGCCTGGGCA
AACATAATTACTGCCGGAATCCTGATGGGGATGCCAAGCCCTGGTG
CCACGTGCTGAAGAACCGCAGGCTGACGTGGGAGTACTGTGATGT
GCCCTCCTGCTCCACCTGCGGCCTGAGACAGTACAGCCAGCCTCAG
TTTCGCATCAAAGGAGGGCTCTTCGCCGACATCGCCTCCCACCCCT
GGCAGGCTGCCATCTTTGCCAAGCACAGGAGGTCGCCCCGGAGAGC
GGTTCCTGTGCGGGGGCATACTCATCAGCTCCTGCTGGATTCTCTCT
GCCGCCCACTGCTTCCAGGAGAGGTTTCCGCCCCACCACCTGACGG
TGATCTTGCGGCAGAACATAACCGGGTGGTCCCTGGCGAGGAGGAGC
AGAAATTTGAAGTCGAAAAATACATTGTCCATAAGGAATTCGATGA

TGACACTTACGACAATGACATTGCGCTGCTGCAGCTGAAATCGGAT
TCGTCCCGCTGTGCCCAGGAGAGCAGCGTGGTCCGCACTGTGTGCC
TTCCCCCGGCGGACCTGCAGCTGCCGGACTGGACGGAGTGTGAGCT
CTCCGGCTACGGCAAGCATGAGGCCTTGTCTCCTTTCTATTCGGAG
CGGCTGAAGGAGGCTCATGTCAGACTGTACCCATCCAGCCGCTGCA
CATCACAACATTTACTTAACAGAACAGTCACCGACAACATGCTGTG
TGCTGGAGACACTCGGAGCGGCGGGCCCCAGGCAAACCTGCACGA
CGCCTGCCAGGGCGATTCGGGAGGCCCCCTGGTGTGTCTGAACGAT
GGCCGCATGACTTTGGTGGGCATCATCAGCTGGGGCCTGGGCTGTG
GACAGAAGGATGTCCCGGGTGTGTACACAAAGGTTACCAACTACCT
AGACTGGATTCTGTGACAACATGCGACCG (SEQ ID NO:2)

8. Method according to one of claims 1 to 7, characterised in that the DNA Sequence of OmpA comprises the following sequence:

ATGAAAAAGACAGCTATCGCGATTGCAGTGGCACTGGCTGGTTTCG
CTACCGTGGCCCAGGCGGCC (SEQ ID NO:3)

9. Method according to one of claims 1 to 8, characterised in that the DNA Sequence of OmpA consists of the following sequence:

ATGAAAAAGACAGCTATCGCGATTGCAGTGGCACTGGCTGGTTTCG
CTACCGTGGCCCAGGCGGCC (SEQ ID NO:3)

10. Method according to one of claims 1 to 9, characterised in that the DNA of the tPA, tPA variant, K2S molecule or K2S variant is preceded by a lac promotor and/or a ribosomal binding site.

11. Method according to one of claims 1 to 10, characterised in that the DNA coding for the tPA, tPA variant, K2S molecule or K2S variant is selected from the group of DNA molecules coding for at least 90% of the amino acids 87 – 527, 174 – 527, 180 – 527 or 220 – 527 of the human tissue plasminogen activator protein.

12. Method according to one of claims 5 to 11, characterised in that the DNA Sequence of K2S comprises the following sequence or a functional variant thereof or a variant due to the degenerate nucleotide code:

TCTGAGGGAAACAGTGACTGCTACTTTGGGAATGGGTCAGCCTACC
GTGGCACGCACAGCCTCACCGAGTCGGGTGCCTCCTGCCTCCCGTG
GAATTCCATGATCCTGATAGGCAAGGTTTACACAGCACAGAACCCC
AGTGCCCAGGCACTGGGCCTGGGCAAACATAATTACTGCCGGAATC
CTGATGGGGATGCCAAGCCCTGGTGCCACGTGCTGAAGAACCGCA
GGCTGACGTGGGAGTACTGTGATGTGCCCTCCTGCTCCACCTGCGG
CCTGAGACAGTACAGCCAGCCTCAGTTTCGCATCAAAGGAGGGCTC
TTCGCCGACATCGCCTCCCACCCCTGGCAGGCTGCCATCTTTGCCA
AGCACAGGAGGTCGCCCCGAGAGCGGTTCTGTGCGGGGGCATACT
TCATCAGCTCCTGCTGGATTCTCTCTGCCGCCCCTGCTTCCAGGAG
AGGTTTCCGCCCCACCACTGACGGTGATCTTGGGCAGAACATAACC
GGGTGGTCCCTGGCGAGGAGGAGCAGAAATTTGAAGTCGAAAAAT
ACATTGTCCATAAGGAATTCGATGATGACACTTACGACAATGACAT
TGCGCTGCTGCAGCTGAAATCGGATTCGTCCCGCTGTGCCAGGAG
AGCAGCGTGGTCCGCACTGTGTGCCTTCCCCCGGCGGACCTGCAGC
TGCCGGACTGGACGGAGTGTGAGCTCTCCGGCTACGGCAAGCATG
AGGCCTTGTCTCCTTTCTATTTCGGAGCGGCTGAAGGAGGCTCATGT
CAGACTGTACCCATCCAGCCGCTGCACATCACAACATTTACTTAAC
AGAACAGTCACCGACAACATGCTGTGTGCTGGAGACACTCGGAGC
GGCGGGCCCCAGGCAAACCTTGACGACGCCTGCCAGGGCGATTTCG
GGAGGGCCCCCTGGTGTGTCTGAACGATGGCCGCATGACTTTGGTGG
GCATCATCAGCTGGGGCCTGGGCTGTGGACAGAAGGATGTCCCGG
GTGTGTACACAAAGGTTACCAACTACCTAGACTGGATTCGTGACAA
CATGCGACCGTGA (SEQ ID NO:4).

13. Method according to one of claims 5 to 12, characterised in that the DNA Sequence of K2S consists of the following sequence:

TCTGAGGGAAACAGTGACTGCTACTTTGGGAATGGGTCAGCCTACC
GTGGCACGCACAGCCTCACCGAGTCGGGTGCCTCCTGCCTCCCGTG
GAATTCCATGATCCTGATAGGCAAGGTTTACACAGCACAGAACCCC
AGTGCCCAGGCACTGGGCCTGGGCAAACATAATTACTGCCGGAATC
CTGATGGGGATGCCAAGCCCTGGTGCCACGTGCTGAAGAACCGCA
GGCTGACGTGGGAGTACTGTGATGTGCCCTCCTGCTCCACCTGCGG
CCTGAGACAGTACAGCCAGCCTCAGTTTCGCATCAAAGGAGGGCTC
TTCGCCGACATCGCCTCCCACCCCTGGCAGGCTGCCATCTTTGCCA
AGCACAGGAGGTGCCCCGAGAGCGGTTCTGTGCGGGGGCATACT
TCATCAGCTCCTGCTGGATTCTCTCTGCCGCCCCACTGCTTCCAGGAG
AGGTTTCCGCCCCACCACCTGACGGTGATCTTGGGCAGAACATACC
GGGTGGTCCCTGGCGAGGAGGAGCAGAAATTTGAAGTCGAAAAT
ACATTGTCCATAAGGAATTCGATGATGACACTTACGACAATGACAT
TGCGCTGCTGCAGCTGAAATCGGATTCGTCCCGCTGTGCCAGGAG
AGCAGCGTGGTCCGCACTGTGTGCCTTCCCCCGGCGGACCTGCAGC
TGCCGGACTGGACGGAGTGTGAGCTCTCCGGCTACGGCAAGCATG
AGGCCTTGTCTCCTTTCTATTCGGAGCGGCTGAAGGAGGCTCATGT
CAGACTGTACCCATCCAGCCGCTGCACATCACAACATTTACTTAAC
AGAACAGTCACCGACAACATGCTGTGTGCTGGAGACACTCGGAGC
GGCGGGCCCCAGGCAAACCTGCACGACGCCTGCCAGGGCGATTCTG
GGAGGCCCCCTGGTGTGTCTGAACGATGGCCGCATGACTTTGGTGG
GCATCATCAGCTGGGGCCTGGGCTGTGGACAGAAGGATGTCCCGG
GTGTGTACACAAAGGTTACCAACTACCTAGACTGGATTCGTGACAA
CATGCGACCGTGA (SEQ ID NO:4).

14. DNA molecule characterized in that it is coding for:

a) the OmpA protein or a functional derivative thereof operably
linked to

b) a DNA molecule coding for a polypeptide containing the
kringle 2 domain and the serine protease domain of tissue plasminogen
activator protein.

15. DNA molecule according to claim 14, characterized in that said DNA sequence comprises the following sequence or a functional variant thereof or a variant due to the degenerate nucleotide code:

ATGAAAAAGACAGCTATCGCGATTGCAGTGGCACTGGCTGGTTTCG
CTACCGTGGCCCAGGCGGCCTCTGAGGGAAACAGTGACTGCTACTT
TGGGAATGGGTCAGCCTACCGTGGCACGCACAGCCTCACCGAGTCG
GGTGCCTCCTGCCTCCCGTGGAATTCCATGATCCTGATAGGCAAGG
TTTACACAGCACAGAACCCCAAGTGCCCAGGCACTGGGCCTGGGCA
AACATAATTACTGCCGGAATCCTGATGGGGATGCCAAGCCCTGGTG
CCACGTGCTGAAGAACCGCAGGCTGACGTGGGAGTACTGTGATGT
GCCCTCCTGCTCCACCTGCGGCCTGAGACAGTACAGCCAGCCTCAG
TTTCGCATCAAAGGAGGGCTCTTCGCCGACATCGCCTCCCACCCCT
GGCAGGCTGCCATCTTTGCCAAGCACAGGAGGTCGCCCCGGAGAGC
GGTTCCTGTGCGGGGGCATACTCATCAGCTCCTGCTGGATTCTCTCT
GCCGCCCCTGCTTCCAGGAGAGGTTTCCGCCCCACCACTGACGG
TGATCTTGGGCAGAACATAACCGGGTGGTCCCTGGCGAGGAGGAGC
AGAAATTTGAAGTCGAAAAATACATTGTCCATAAGGAATTCGATGA
TGACACTTACGACAATGACATTGCGCTGCTGCAGCTGAAATCGGAT
TCGTCCCGCTGTGCCCAGGAGAGCAGCGTGGTCCGCACTGTGTGCC
TTCCCCCGGCGGACCTGCAGCTGCCGGACTGGACGGAGTGTGAGCT
CTCCGGCTACGGCAAGCATGAGGCCTTGTCTCCTTTCTATTTCGGAG
CGGCTGAAGGAGGCTCATGTCAGACTGTACCCATCCAGCCGCTGCA
CATCACAACATTTACTTAACAGAACAGTCACCGACAACATGCTGTG
TGCTGGAGACACTCGGAGCGGCGGGCCCCAGGCAAACCTTGACGA
CGCCTGCCAGGGCGATTTCGGGAGGGCCCCCTGGTGTGTCTGAACGAT
GGCCGCATGACTTTGGTGGGCATCATCAGCTGGGGCCTGGGCTGTG
GACAGAAGGATGTCCCGGGTGTGTACACAAAGGTTACCAACTACCT
AGACTGGATTCGTGACAACATGCGACCG (SEQ ID NO:5).

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16. DNA molecule according to claim 14 or 15, characterized in that said DNA sequence consists of the following sequence:

ATGAAAAAGACAGCTATCGCGATTGCAGTGGCACTGGCTGGTTTCG
CTACCGTGGCCCAGGCGGCCTCTGAGGGAAACAGTGACTGCTACTT
TGGGAATGGGTCAGCCTACCGTGGCACGCACAGCCTCACCGAGTCG
GGTGCCTCCTGCCTCCCGTGGAATTCCATGATCCTGATAGGCAAGG
TTTACACAGCACAGAACCCCAAGTGCCCAGGCACTGGGCCTGGGCA
AACATAATTACTGCCGGAATCCTGATGGGGATGCCAAGCCCTGGTG
CCACGTGCTGAAGAACCGCAGGCTGACGTGGGAGTACTGTGATGT
GCCCTCCTGCTCCACCTGCGGCCTGAGACAGTACAGCCAGCCTCAG
TTTCGCATCAAAGGAGGGCTCTTCGCCGACATCGCCTCCCACCCCT
GGCAGGCTGCCATCTTTGCCAAGCACAGGAGGTCGCCCCGGAGAGC
GGTTCCTGTGCGGGGGCATACTCATCAGCTCCTGCTGGATTCTCTCT
GCCGCCCACTGCTTCCAGGAGAGGTTTCCGCCCCACCACCTGACGG
TGATCTTGGGCAGAACATAACCGGGTGGTCCCTGGCGAGGAGGAGC
AGAAATTTGAAGTCGAAAAATACATTGTCCATAAGGAATTCGATGA
TGACACTTACGACAATGACATTGCGCTGCTGCAGCTGAAATCGGAT
TCGTCCCCGCTGTGCCCAGGAGAGCAGCGTGGTCCGCACTGTGTGCC
TTCCCCCGGCGGACCTGCAGCTGCCGGACTGGACGGAGTGTGAGCT
CTCCGGCTACGGCAAGCATGAGGCCTTGTCTCCTTTCTATTTCGGAG
CGGCTGAAGGAGGCTCATGTCAGACTGTACCCATCCAGCCGCTGCA
CATCACAACATTTACTTAACAGAACAGTCACCGACAACATGCTGTG
TGCTGGAGACACTCGGAGCGGCGGGCCCCAGGCAAACCTTGACGA
CGCCTGCCAGGGCGATTTCGGGAGGCCCCCTGGTGTGTCTGAACGAT
GGCCGCATGACTTTGGTGGGCATCATCAGCTGGGGCCTGGGCTGTG
GACAGAAGGATGTCCCGGGTGTGTACACAAAGGTTACCAACTACCT
AGACTGGATTTCGTGACAACATGCGACCG (SEQ ID NO:5).

17. DNA molecule according to one of claims 14 to 16, characterized in that said DNA sequence b) is coding for at least 90% of the amino acids 87 – 527 of the human tissue plasminogen activator protein.

18. DNA molecule according to one of claims 14 to 17, characterized in that said DNA sequence b) is coding for at least 90% of the amino acids 174 – 527 of the human tissue plasminogen activator protein.

19. DNA molecule according to any one of claims 14 to 18, characterized in that said DNA sequence b) is coding for at least 90% of the amino acids 180 – 527 of the human tissue plasminogen activator protein.

20. DNA molecule according to any one of claims 14 to 19, characterized in that said DNA sequence b) is coding for at least 90% of the amino acids 220 – 527 of the human tissue plasminogen activator protein.

21. DNA molecule according to any one of claims 14 to 20, characterized in that said DNA sequence a) is hybridizing under stringent conditions to the following sequence:

ATGAAAAAGACAGCTATCGCGATTGCAGTGGCACTGGCTGGTTTCG
CTACCGTGGCCCAGGCGGCC (SEQ ID NO:6).

22. DNA molecule according to any one of claims 14 to 21, characterized in that said DNA sequence a) consists of the following sequence:

ATGAAAAAGACAGCTATCGCGATTGCAGTGGCACTGGCTGGTTTCG
CTACCGTGGCCCAGGCGGCC (SEQ ID NO:6).

23. DNA molecule according to any one of claims 14 to 22, characterized in that said DNA sequence b) is hybridizing under stringent conditions to the following sequence:

TCTGAGGGAAACAGTGACTGCTACTTTGGGAATGGGTCAGCCTACC
GTGGCACGCACAGCCTCACCGAGTCGGGTGCCTCCTGCCTCCCGTG
GAATTCCATGATCCTGATAGGCAAGGTTTACACAGCACAGAACCCC

AGTGCCCAGGCACTGGGCCTGGGCAAACATAATTACTGCCGGAATC
CTGATGGGGATGCCAAGCCCTGGTGCCACGTGCTGAAGAACCGCA
GGCTGACGTGGGAGTACTGTGATGTGCCCTCCTGCTCCACCTGCGG
CCTGAGACAGTACAGCCAGCCTCAGTTTTCGCATCAAAGGAGGGCTC
TTCGCCGACATCGCCTCCCACCCCTGGCAGGCTGCCATCTTTGCCA
AGCACAGGAGGTGCCCCGGAGAGCGGTTCTGTGCGGGGGCATAAC
TCATCAGCTCCTGCTGGATTCTCTCTGCCGCCCACTGCTTCCAGGAG
AGGTTTCCGCCCCACCACCTGACGGTGATCTTGGGCAGAACATAACC
GGGTGGTCCCTGGCGAGGAGGAGCAGAAATTTGAAGTCGAAAAAT
ACATTGTCCATAAGGAATTCGATGATGACACTTACGACAATGACAT
TGCGCTGCTGCAGCTGAAATCGGATTCGTCCCGCTGTGCCCAGGAG
AGCAGCGTGGTCCGCACTGTGTGCCTTCCCCCGGCGGACCTGCAGC
TGCCGGACTGGACGGAGTGTGAGCTCTCCGGCTACGGCAAGCATG
AGGCCTTGTCTCCTTTCTATTTCGGAGCGGCTGAAGGAGGCTCATGT
CAGACTGTACCCATCCAGCCGCTGCACATCACAACATTTACTTAAC
AGAACAGTCACCGACAACATGCTGTGTGCTGGAGACACTCGGAGC
GGCGGGCCCCCAGGCAAACCTTGCACGACGCCTGCCAGGGCGATTCTG
GGAGGCCCCCTGGTGTGTCTGAACGATGGCCGCATGACTTTGGTGG
GCATCATCAGCTGGGGCCTGGGCTGTGGACAGAAGGATGTCCCGG
GTGTGTACACAAAGGTTACCAACTACCTAGACTGGATTTCGTGACAA
CATGCGACCGTGA (SEQ ID NO:7).

24. DNA molecule according to any one of claims 14 to 23, characterized in that said DNA sequence b) consists of the following sequence:

TCTGAGGGAAACAGTGACTGCTACTTTGGGAATGGGTCAGCCTACC
GTGGCACGCACAGCCTCACCGAGTCGGGTGCCTCCTGCCTCCCGTG
GAATTCCATGATCCTGATAGGCAAGGTTTACACAGCACAGAACCCC
AGTGCCCAGGCACTGGGCCTGGGCAAACATAATTACTGCCGGAATC
CTGATGGGGATGCCAAGCCCTGGTGCCACGTGCTGAAGAACCGCA
GGCTGACGTGGGAGTACTGTGATGTGCCCTCCTGCTCCACCTGCGG

CCTGAGACAGTACAGCCAGCCTCAGTTTCGCATCAAAGGAGGGCTC
TTCGCCGACATCGCCTCCCACCCCTGGCAGGCTGCCATCTTTGCCA
AGCACAGGAGGTGCCCCGAGAGCGGTTCTGTGCGGGGGCATAAC
TCATCAGCTCCTGCTGGATTCTCTCTGCCGCCCACTGCTTCCAGGAG
AGGTTTCCGCCCCACCACCTGACGGTGATCTTGGGCAGAACATACC
GGGTGGTCCCTGGCGAGGAGGAGCAGAAATTTGAAGTCGAAAAAT
ACATTGTCCATAAGGAATTCGATGATGACACTTACGACAATGACAT
TGCGCTGCTGCAGCTGAAATCGGATTCGTCCCGCTGTGCCCAGGAG
AGCAGCGTGGTCCGCACTGTGTGCCTTCCCCCGGCGGACCTGCAGC
TGCCGGACTGGACGGAGTGTGAGCTCTCCGGCTACGGCAAGCATG
AGGCCTTGTCTCCTTTCTATTTCGGAGCGGCTGAAGGAGGCTCATGT
CAGACTGTACCCATCCAGCCGCTGCACATCACAAACATTTACTTAAC
AGAACAGTCACCGACAACATGCTGTGTGCTGGAGAACTCGGAGC
GGCGGGCCCCAGGCAAACCTTGACGACGCCTGCCAGGGCGATTTCG
GGAGGCCCCCTGGTGTGTCTGAACGATGGCCGCATGACTTTGGTGG
GCATCATCAGCTGGGGCCTGGGCTGTGGACAGAAGGATGTCCCGG
GTGTGTACACAAAGGTTACCAACTACCTAGACTGGATTCGTGACAA
CATGCGACCGTGA (SEQ ID NO:7).

25. Fusion protein of OmpA and K2S, characterised in that it comprises a protein characterized by the following amino acid sequence or a fragment, a functional variant, an allelic variant, a subunit, a chemical derivative or a glycosylation variant thereof:

MKKTAAIAVALAGFATVAQAASEGNSDCYFGNGSAYRGTHSLTESG
ASCLPWNSMILIGKVYTAQNPSAQUALGLGKHNYCRNPDGDAKPWCH
VLKNRRLTWEYCDVPSCSTCGLRQYSQPQFRIKGGLFADIASHPWQA
AIFAKHRRSPGERFLCGGILISSCWILSAAHCFQERFPPHHLTIVLGRTY
RVVPGEEEQKFEVEKYIVHKEFDDDTYDNDIALQLKSDSSRCAQESS
VVRTVCLPPADLQLPDWTECELSGYGKHEALSPFYSERLKEAHVRLYP
SSRCTSQHLLNRTVTDNMLCAGDTRSGGPQANLHDACQGDSGGPLVC

LNDGRMTLVGIISWGLGCGQKDVPGVYTKVTNYLDWIRDNMRPG
(SEQ ID NO:8).

26. Fusion protein of OmpA and K2S according to claim 25, characterised in that it consists of a protein characterized by the following amino acid sequence:

MKKTAIAlAVALAGFATVAQAASEGNSDCYFGNGSAYRGTHSLTESG
ASCLPWNSMILIGKVYTAQNPSAQALGLGKHNYCRNPDGDAKPWCH
VLKNRRLTWEYCDVPSCSTCGLRQYSQPQFRIKGGLFADIASHPWQA
AIFAKHRRSPGERFLCGGILISSCWILSAAHCFQERFPPHHLTIVILGRTY
RVVPGEEEEQKFEVEKYIVHKEFDDDTYDNDIALQLKSDSSRCAQESS
VVRTVCLPPADLQLPDWTECELSGYGKHEALSPFYSERLKEAHVRLYP
SSRCTSQHLLNRTVTDNMLCAGDTRSGGPQANLHDACQGDSGGPLVC
LNDGRMTLVGIISWGLGCGQKDVPGVYTKVTNYLDWIRDNMRPG
(SEQ ID NO:8).

27. K2S protein, characterised in that it comprises a protein defined by the sequence SEGN (SEQ ID NO:9) and a or a variant or a fragment, a functional variant, an allelic variant, a subunit, a chemical derivative, a fusion protein or a glycosylation variant thereof.

28. K2S protein according to claim 27, characterised in that it comprises a protein defined by the sequence SEGNSD (SEQ ID NO:10) and a or a variant or a fragment, a functional variant, an allelic variant, a subunit, a chemical derivative, a fusion protein or a glycosylation variant thereof.

29. K2S protein according to claim 28 or 29, characterised in that it comprises a protein characterized by the following amino acid sequence or a fragment, a functional variant, an allelic variant, a subunit, a chemical derivative or a glycosylation variant thereof:

SEGNSDCYFGNGSA YRGTHSLTESGASCLPWNSMILIGKVYTAQNPSA
QALGLGKHNYCRNPDGDAKPWCHVLKNRRLTWEYCDVPSCSTCGLR
QYSQPQFRIKGGLFADIASHPWQAAIFAKHRRSPGERFLCGGILISSCWI
LSAAHCFQERFPPHHLTIVILGR TYRVVPGE EEQKFEVEKYIVHKEFDD
DTYDNDIAL LQLKSDSSRCAQESSVVRTVCLPPADLQLPDWTECELSG
YGKHEALSPFYSERLKEAHVRLYPSSRCTSQHLLNRTVTDNMLCAGD
TRSGGPQANLHDACQGDSGGPLVCLNDGRMTLVGIISWGLGCGQKD
VPGVYTKVTNYLDWIRDNM RP* (SEQ ID NO:11).

30. K2S according to any one of claims 27 to 30, characterised in that it consists of a protein characterized by the following amino acid sequence:

SEGNSDCYFGNGSA YRGTHSLTESGASCLPWNSMILIGKVYTAQNPSA
QALGLGKHNYCRNPDGDAKPWCHVLKNRRLTWEYCDVPSCSTCGLR
QYSQPQFRIKGGLFADIASHPWQAAIFAKHRRSPGERFLCGGILISSCWI
LSAAHCFQERFPPHHLTIVILGR TYRVVPGE EEQKFEVEKYIVHKEFDD
DTYDNDIAL LQLKSDSSRCAQESSVVRTVCLPPADLQLPDWTECELSG
YGKHEALSPFYSERLKEAHVRLYPSSRCTSQHLLNRTVTDNMLCAGD
TRSGGPQANLHDACQGDSGGPLVCLNDGRMTLVGIISWGLGCGQKD
VPGVYTKVTNYLDWIRDNM RP* (SEQ ID NO:11).

31. A vector containing a DNA sequence according to any one of claims 14 to 24.

32. A vector according to claim 31, wherein said DNA sequence is preceded by a lac promoter and a ribosomal binding site.

33. The vector pComb3HSS containing a DNA according to any one of claims 14 to 24, wherein the expression of the gp III protein is suppressed or inhibited by deleting the DNA molecule encoding said gp III protein or by a stop codon between the gene coding for a polypeptide

containing the kringle 2 domain and the serine protease domain of tissue plasminogen activator protein and the protein III gene.

34. A prokaryotic host cell comprising a DNA molecule according to any one of claims 14 to 24.

35. A prokaryotic host cell comprising a vector according to any one of claims 31 to 33.

36. An *E. coli* host cell comprising a DNA molecule according to any one of claims 14 to 24.

37. An *E. coli* host cell comprising a vector according to any one of claims 31 to 33.

38. Use of a DNA molecule according to any one of claims 14 to 24 or of a vector according to any one of claims 31 to 33 or a host cell according to any one of claims 34 to 37 in a method for the production of a polypeptide having the activity of tissue plasminogen activator.

39. Use according to claim 38, wherein said method is a method according to any one of claims 1 to 13.